

## 2/32

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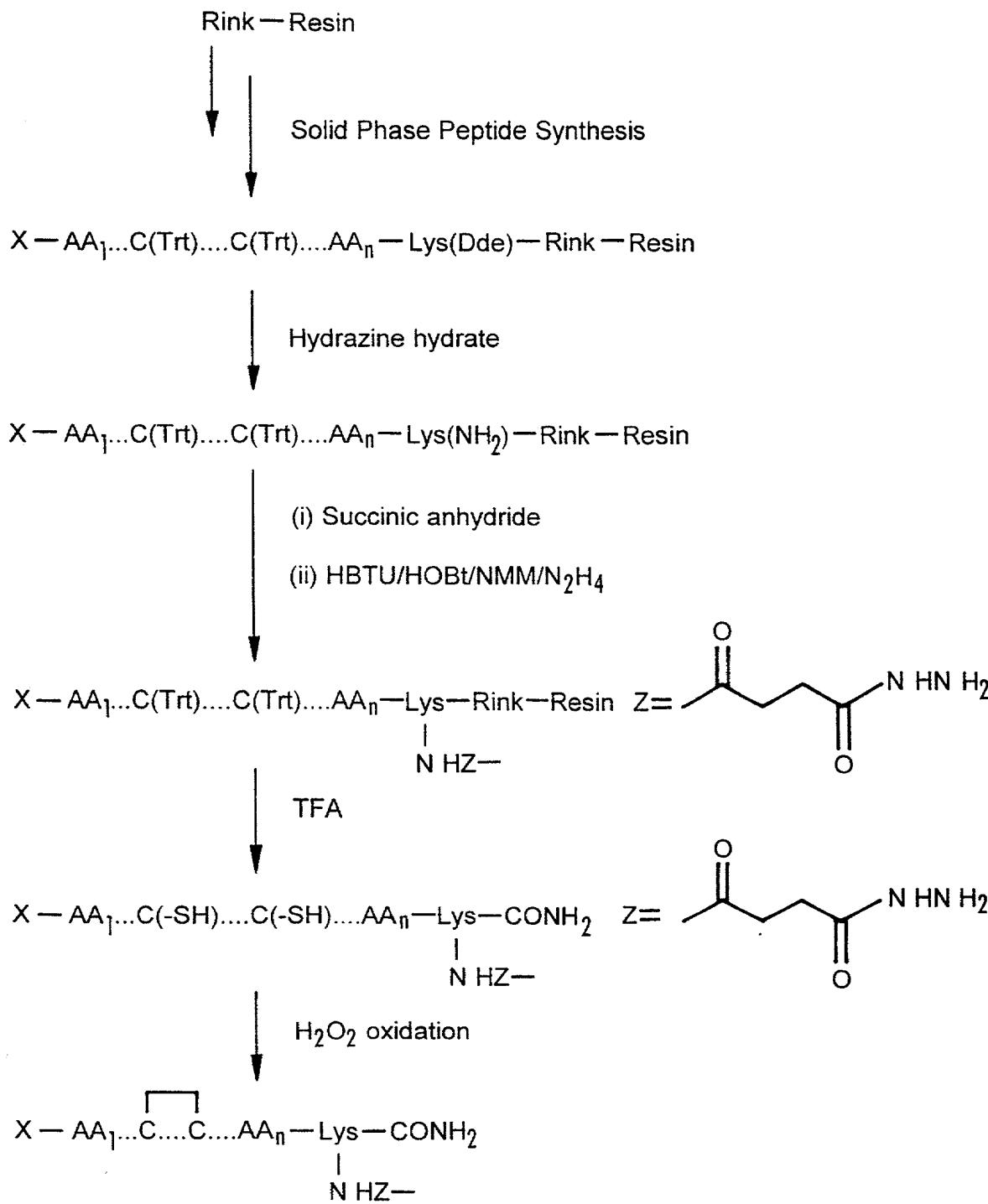
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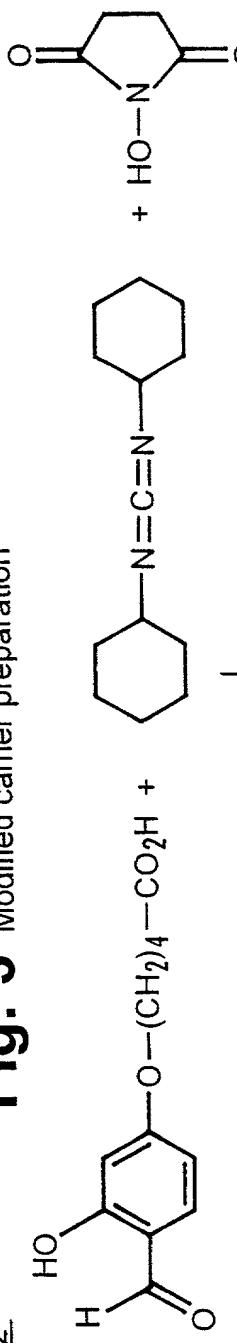
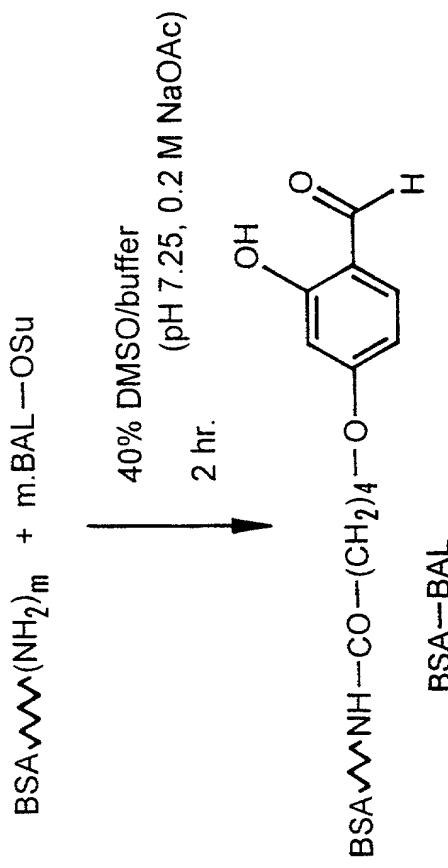
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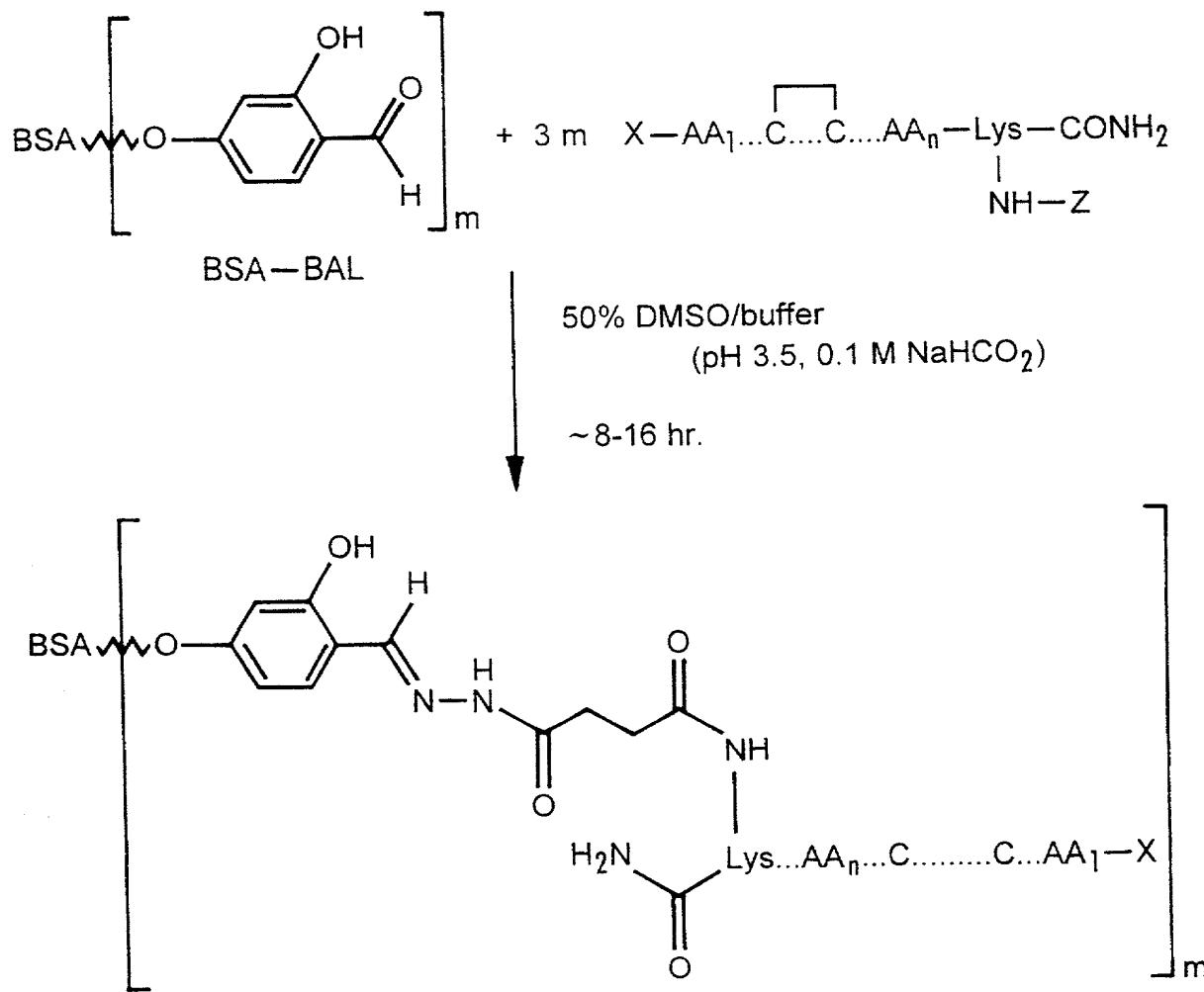
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**Fig. 2** Scheme 1, solid phase peptide synthesisScheme 1

**Scheme 2****Scheme 3**

**Fig. 4** Chemistry Scheme 4, Peptide/carrier conjugation

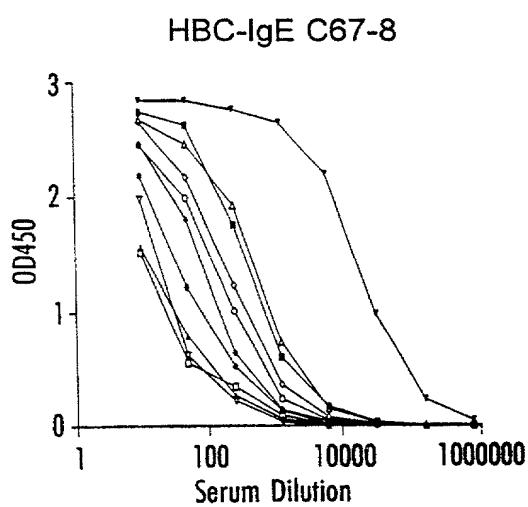
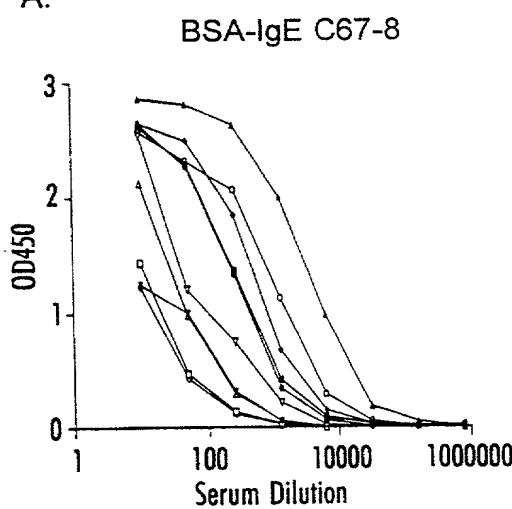
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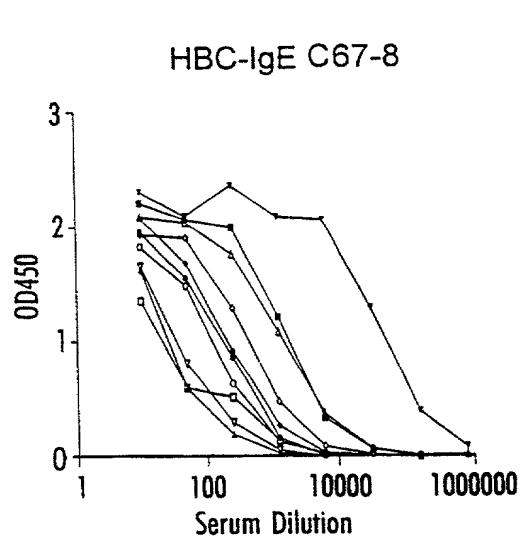
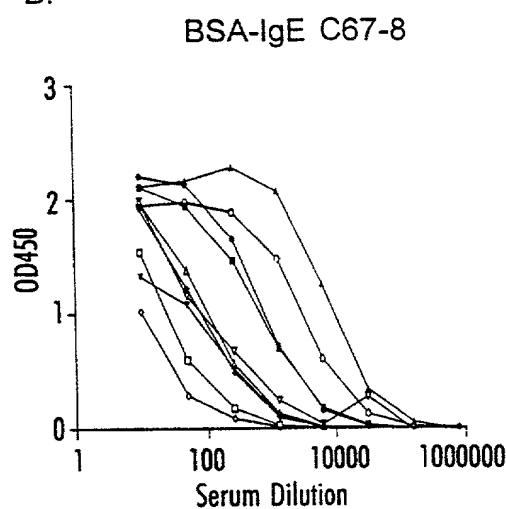
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**Fig. 5** C67-8 Anti-IgE Data

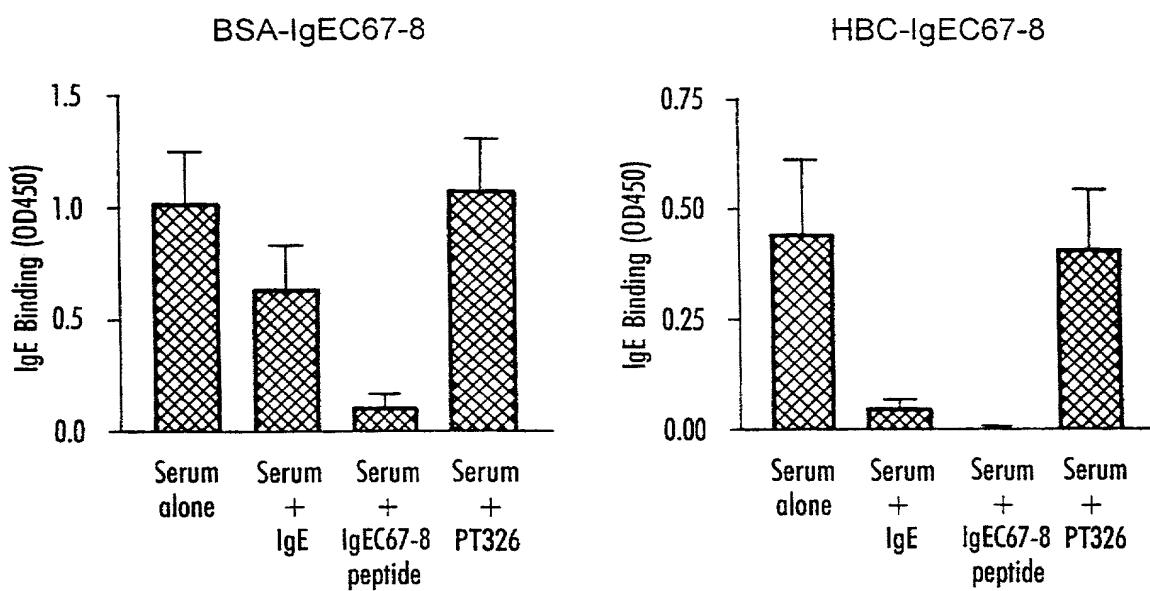
A.



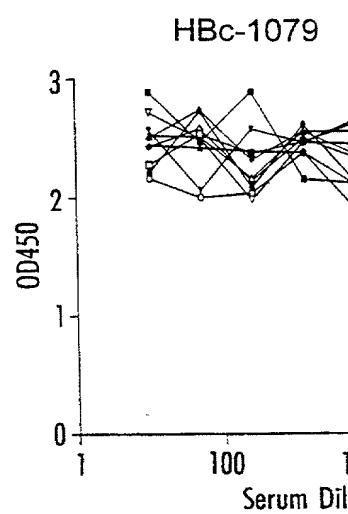
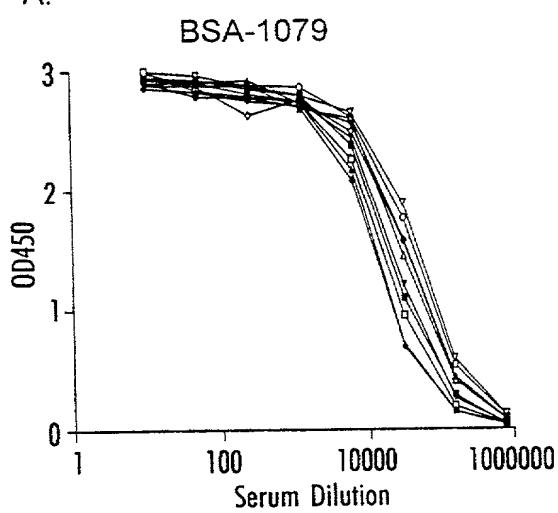
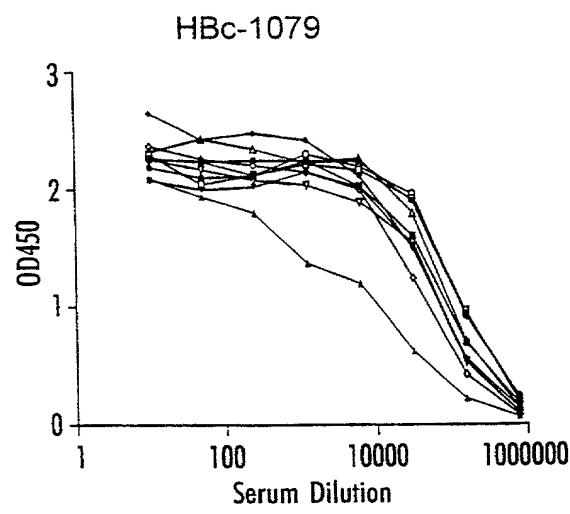
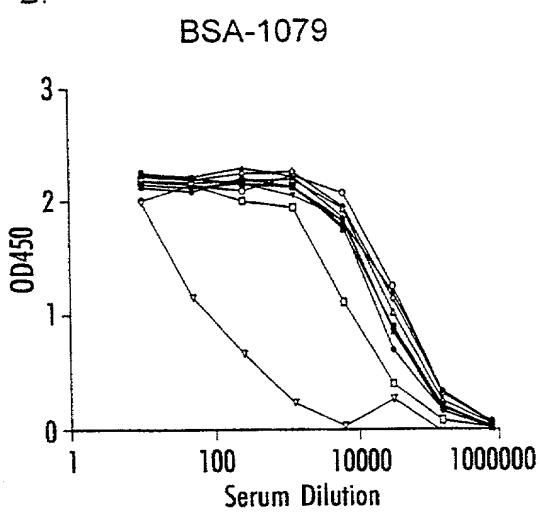
B.



**Fig. 6** Competition assay with soluble IgE and IgE C67-8 peptide.

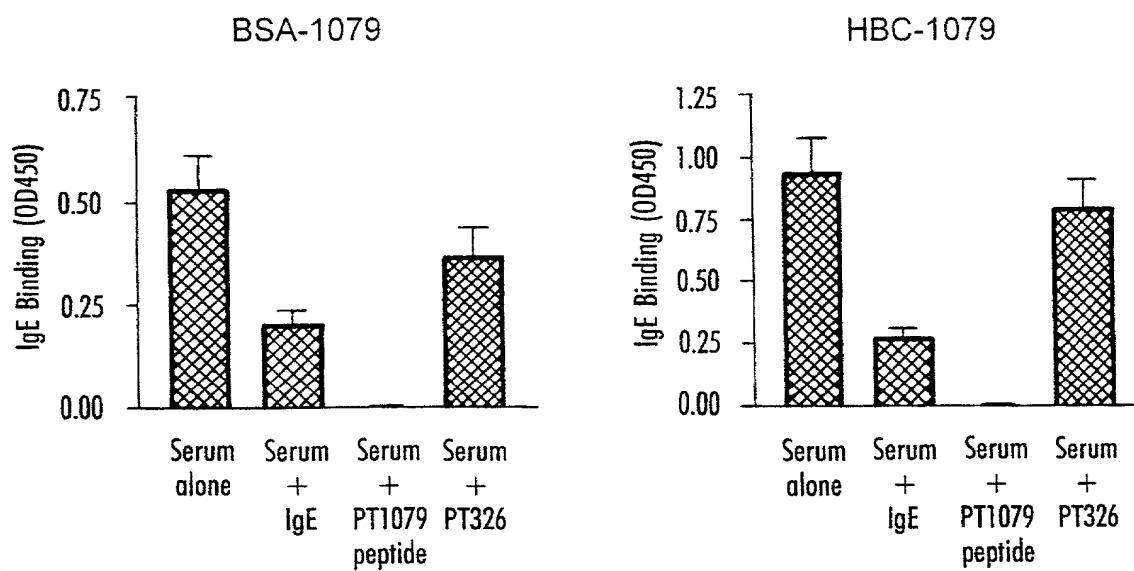


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**Fig. 7** PT1079 Anti-IgE Data**A.****B.**

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**Fig. 8** Competition assay with soluble IgE and PT1079 peptide.



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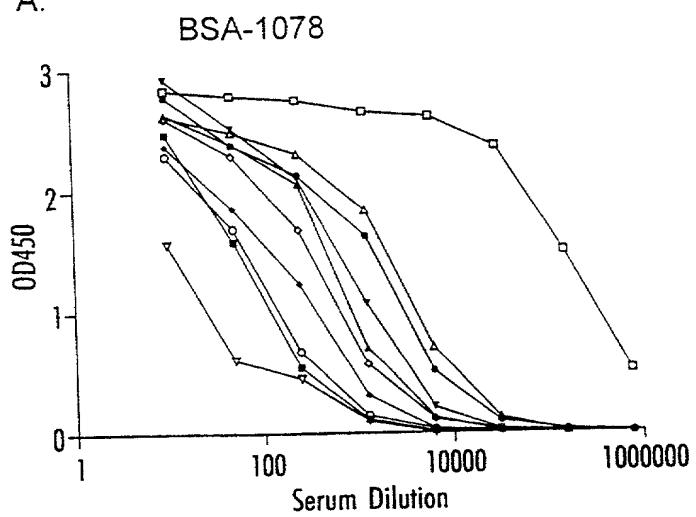
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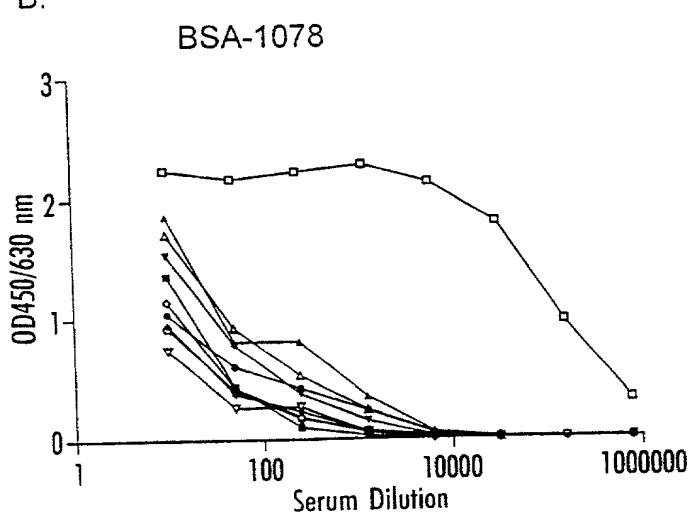
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**Fig. 9** PT1078 Anti-IgE Data

A.

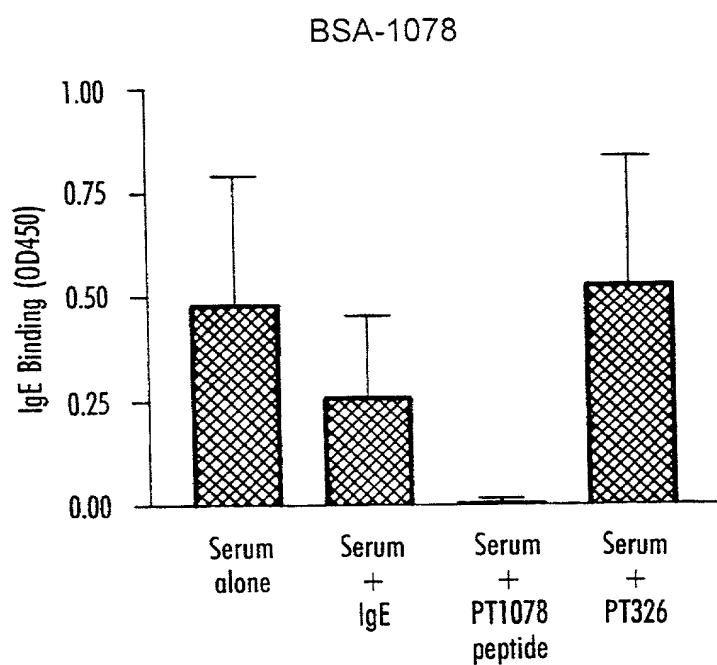


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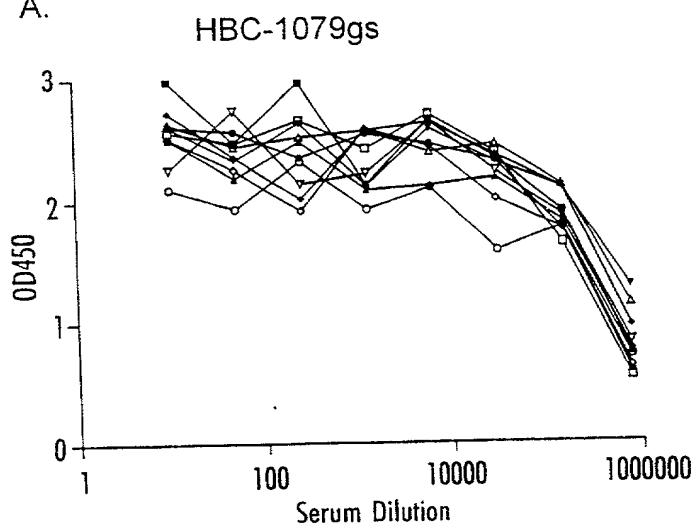
**Fig. 10** Competition assay with soluble IgE and PT1078 peptide.



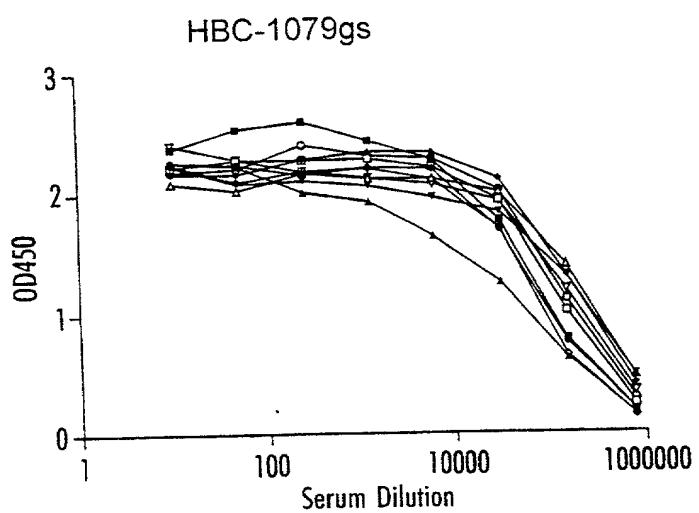
13/32

**Fig. 11** PT1079gs Anti-IgE Data

A.

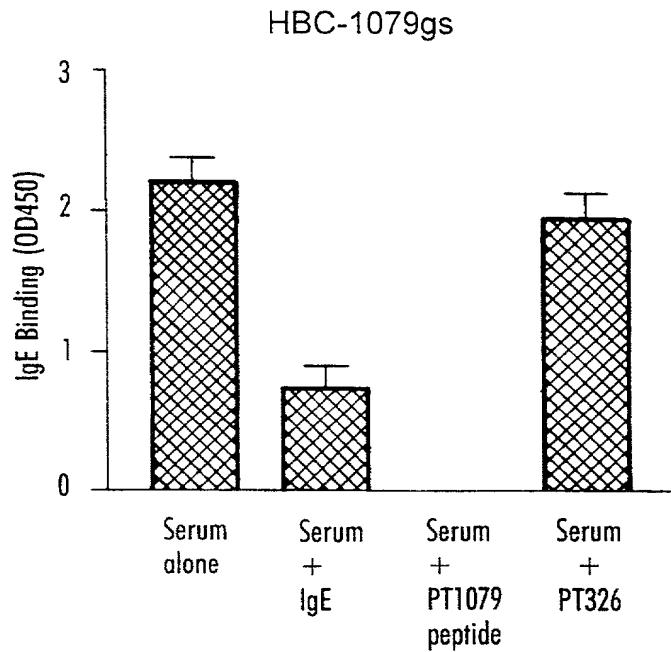


B.

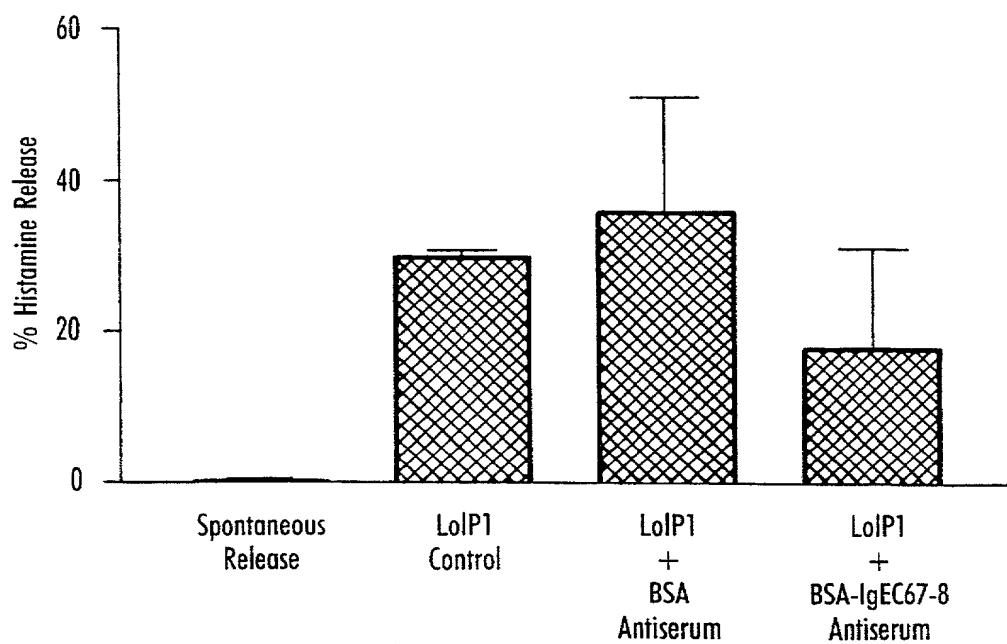


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**Fig. 12** Competition assay with soluble IgE and PT1079 peptide.

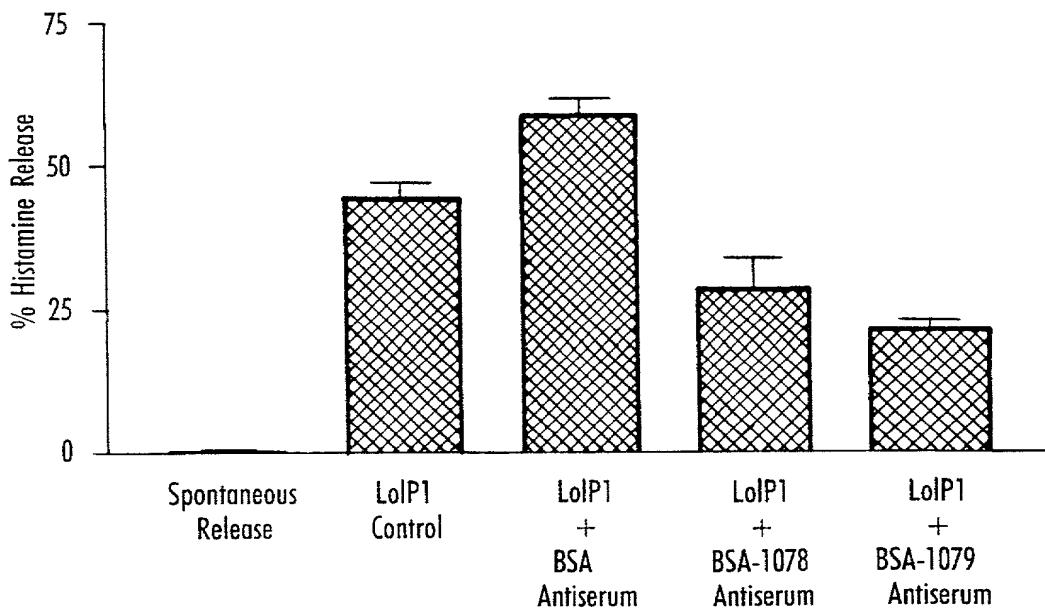


**Fig. 13** Inhibitory Activity of Mouse BSA-C67-8 induced Antisera

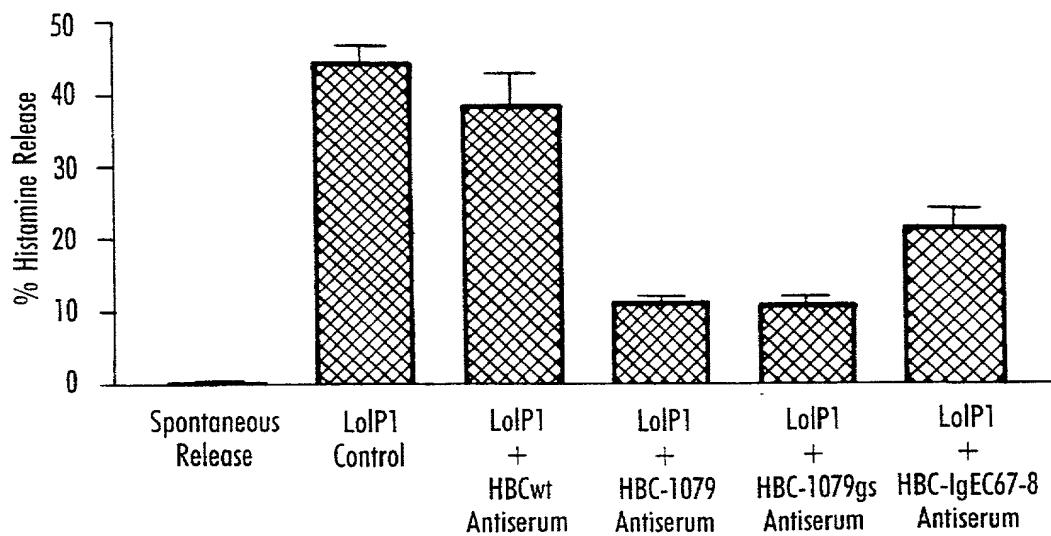


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**Fig. 14** Inhibitory Activity of Mouse Antisera induced by BSA-1078 and BSA-1079.

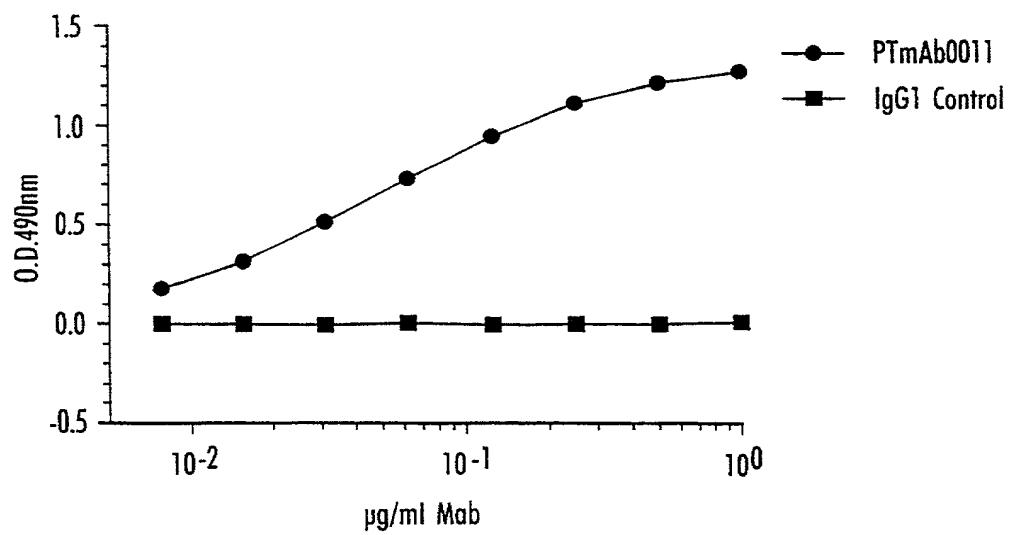
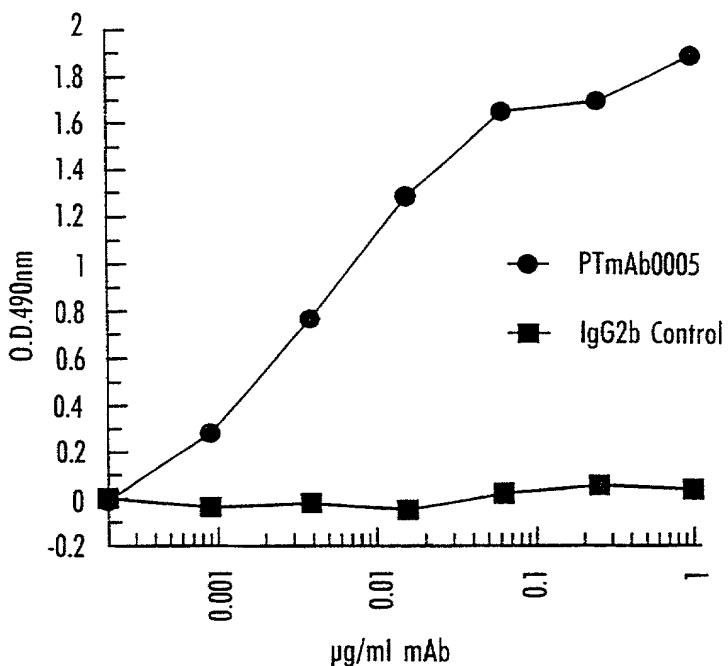


**Fig. 15** Inhibitory Activity of Mouse Antisera induced by HBC-C67-8, HBC-1078, HBC-1079 and HBC-1079gs



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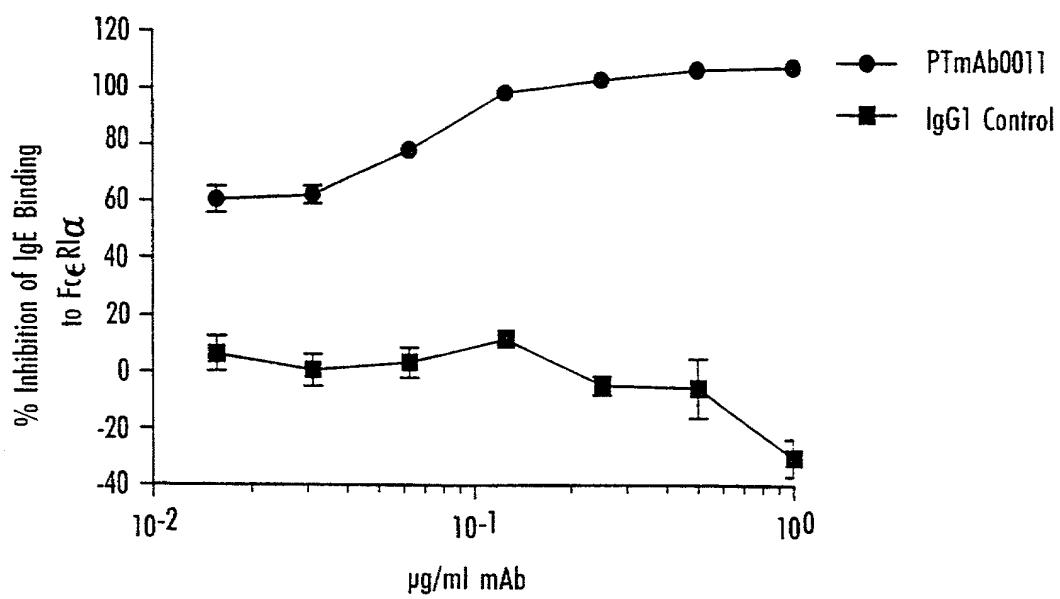
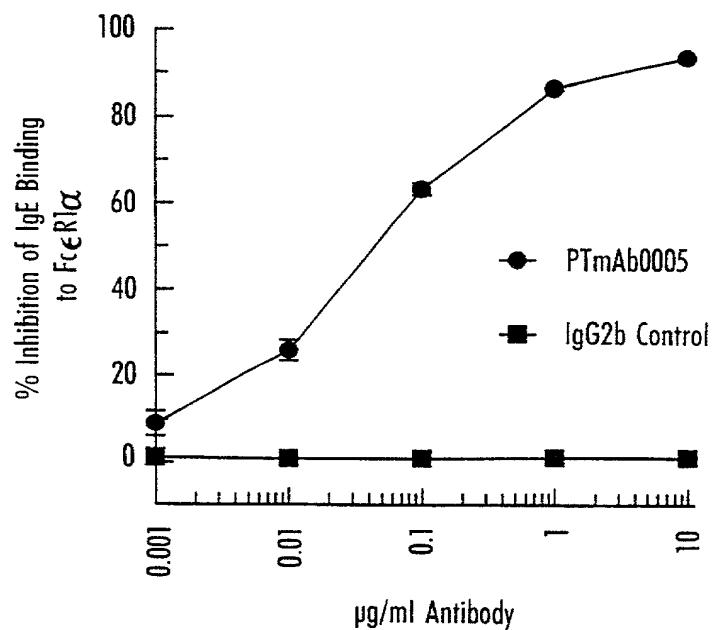
**Fig. 16** shows the concentration dependent binding of antibody PTmAb0005 and PTmAb0011 to IgE.



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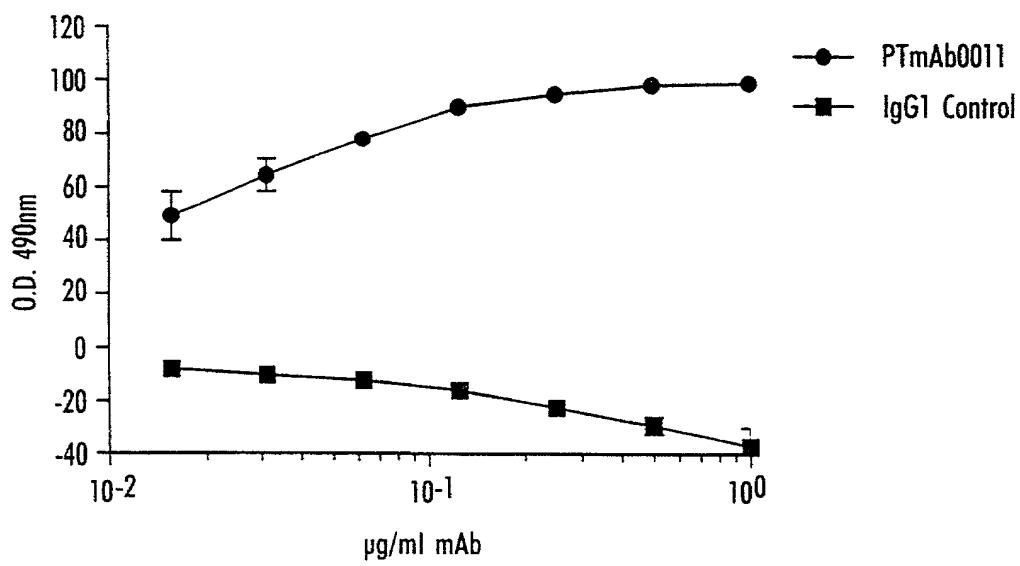
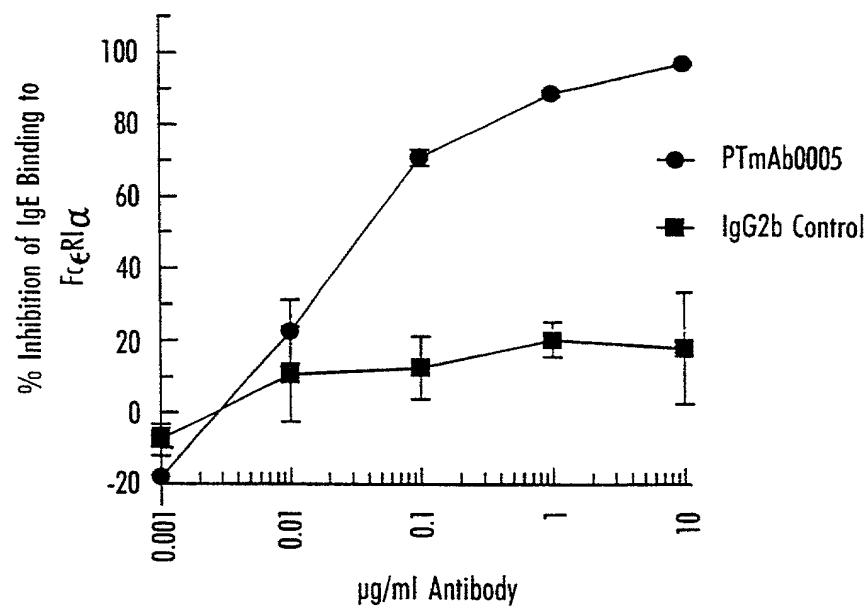
**Fig. 17**

shows the concentration dependent inhibition of IgE binding to an Fc $\epsilon$ R1 $\alpha$ /IgG construct with antibody PTmAb0005 and PTmAb0011 compared to control.



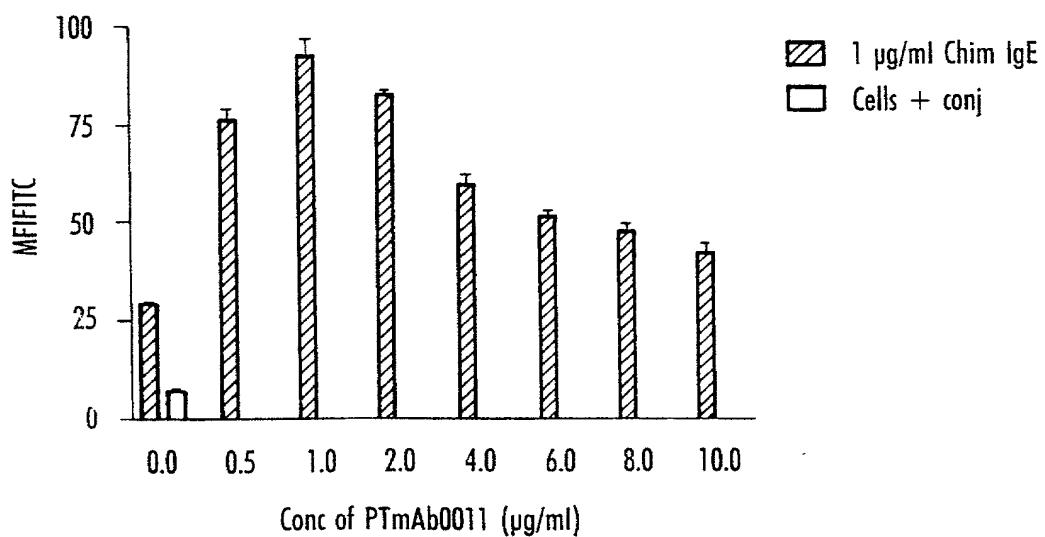
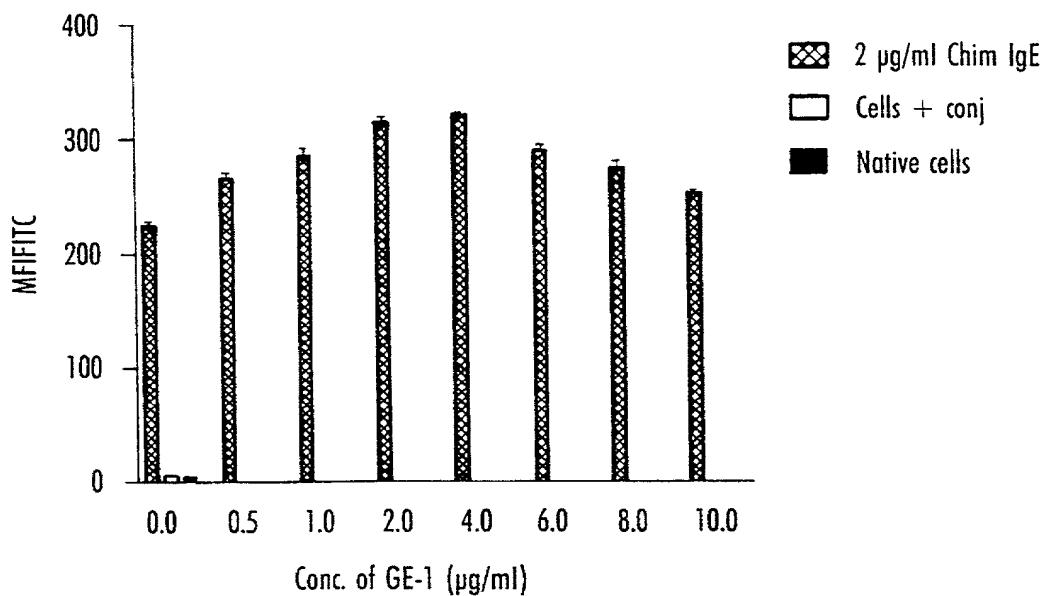
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**Fig. 18** shows the concentration dependent inhibition of IgE binding to clipped ectodomain of Fc $\epsilon$ RI $\alpha$ -bound directly to plastic plates, by antibody PTmAb0005, compared to control.



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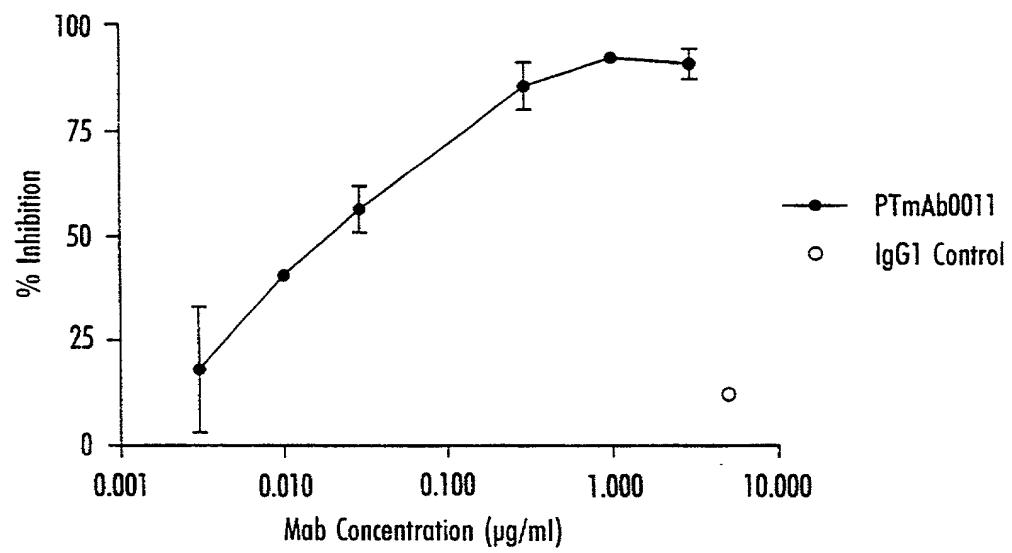
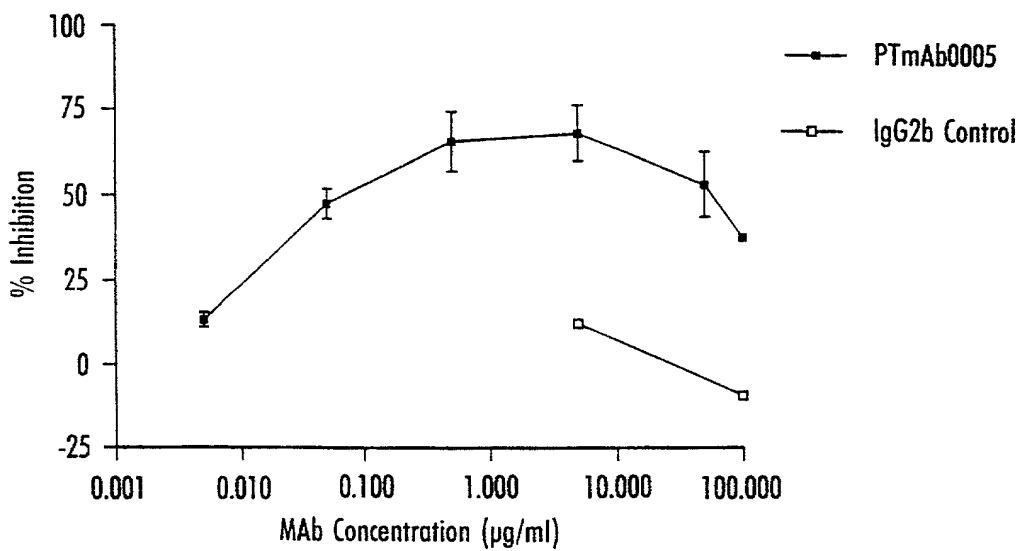
**Fig. 19** shows IgE binding to Fc $\epsilon$ RII (CD23) by antibody PTmAb0005 (GE-1) and PTmAb0011.



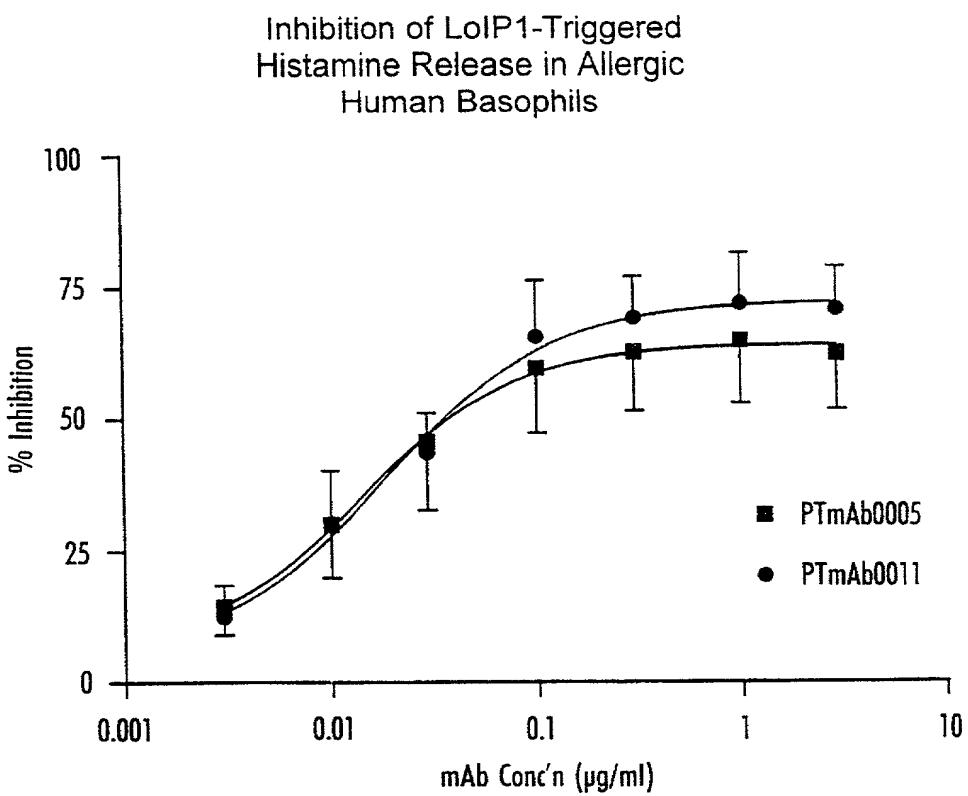
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**Fig. 20**

shows the concentration-dependent blocking of histamine release from allergic human blood basophils with antibody PTmAb0005 and PTmAb0011 compared to control.



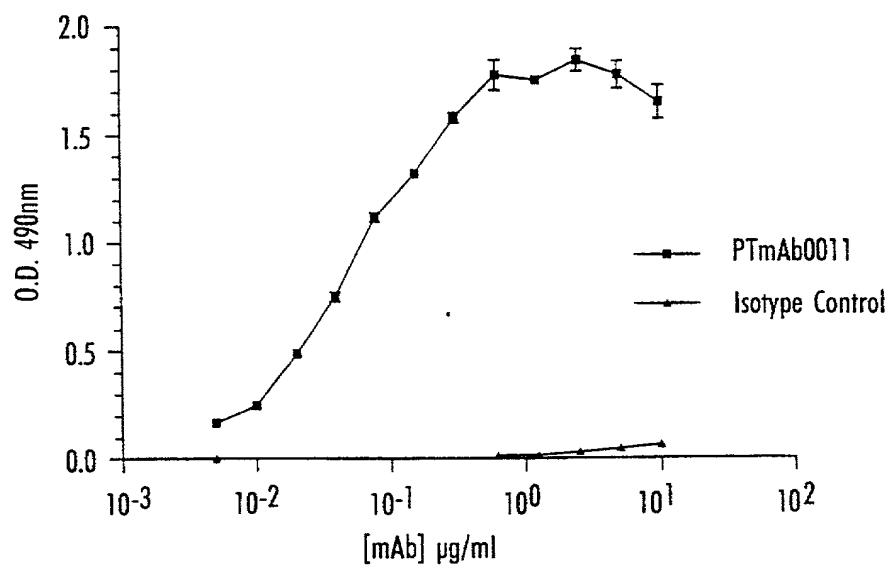
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**Fig. 21**

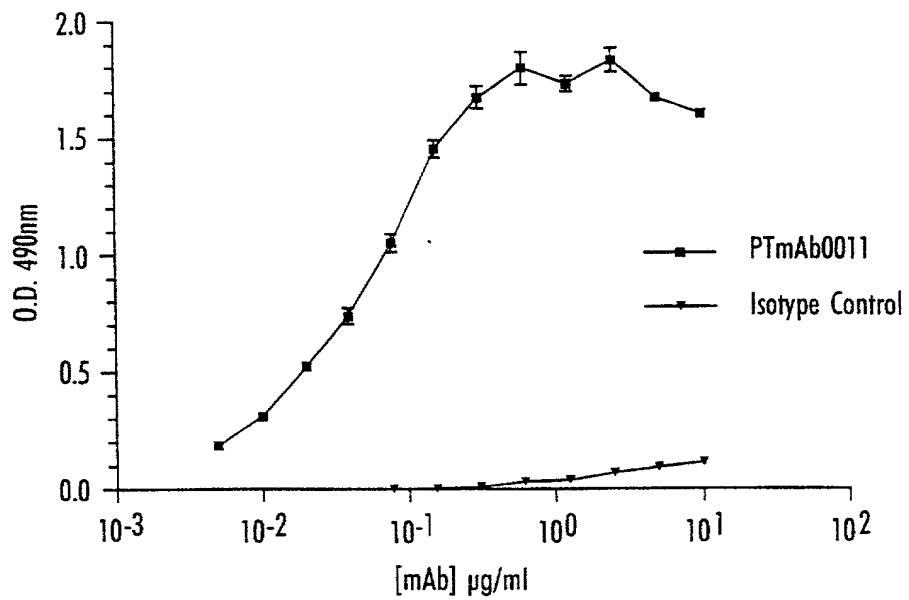
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**Fig. 22** PTmAb0011 binding to different IgE.

## A. Chimaeric IgE



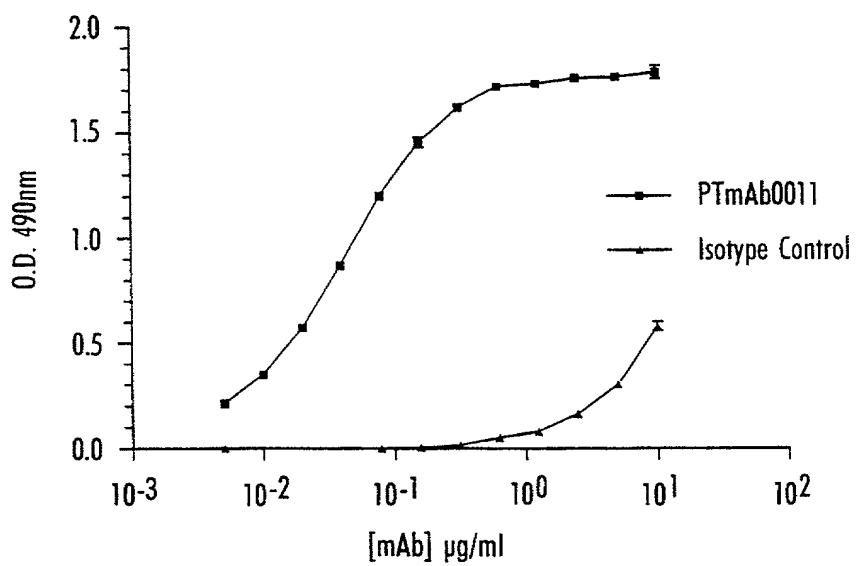
## B. Binding to Myeloma IgE



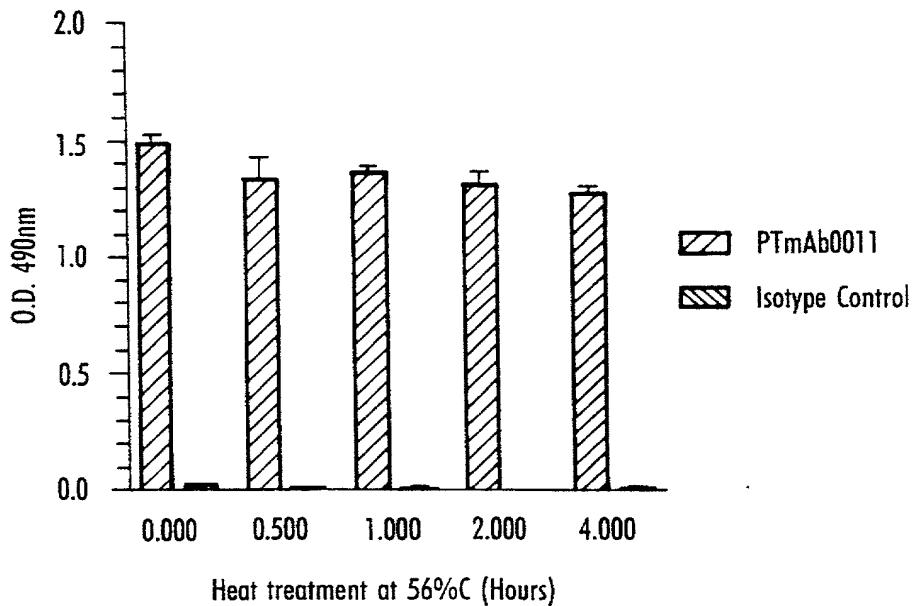
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**Fig. 22**

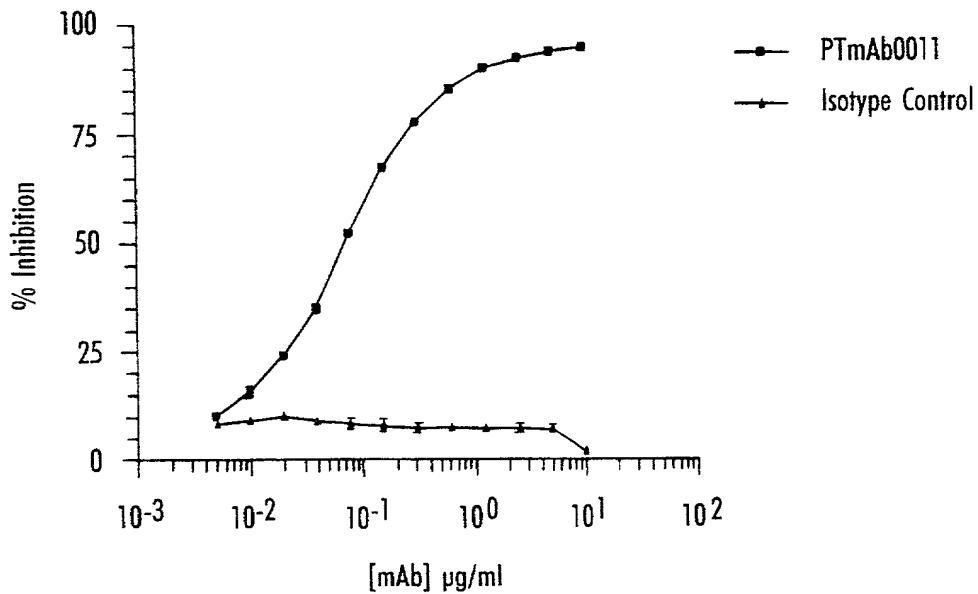
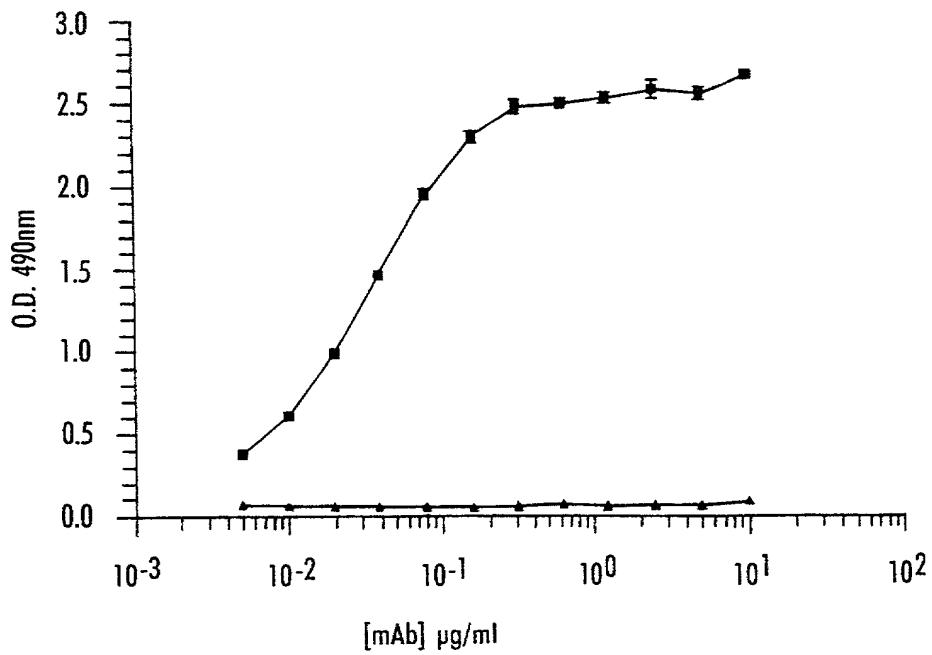
## C. Binding to Antigen Orientated IgE



## D. Binding to Heat Denatured IgE



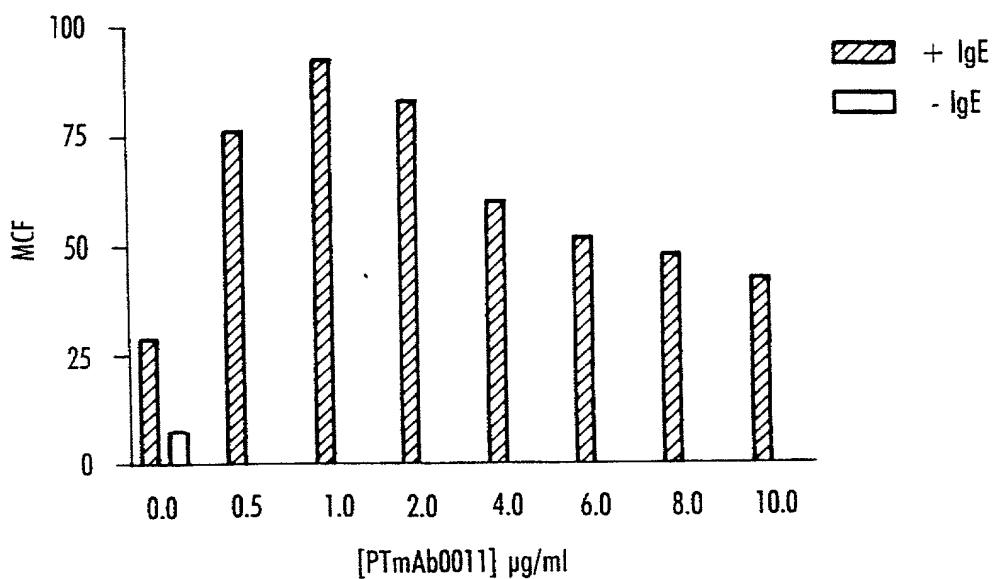
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**Fig. 23** Inhibition of IgE Binding to Fc $\epsilon$ R1 $\alpha$  by PTmAb0011.**Fig. 24** Binding of PTmAb0011 to Receptor Bound IgE.

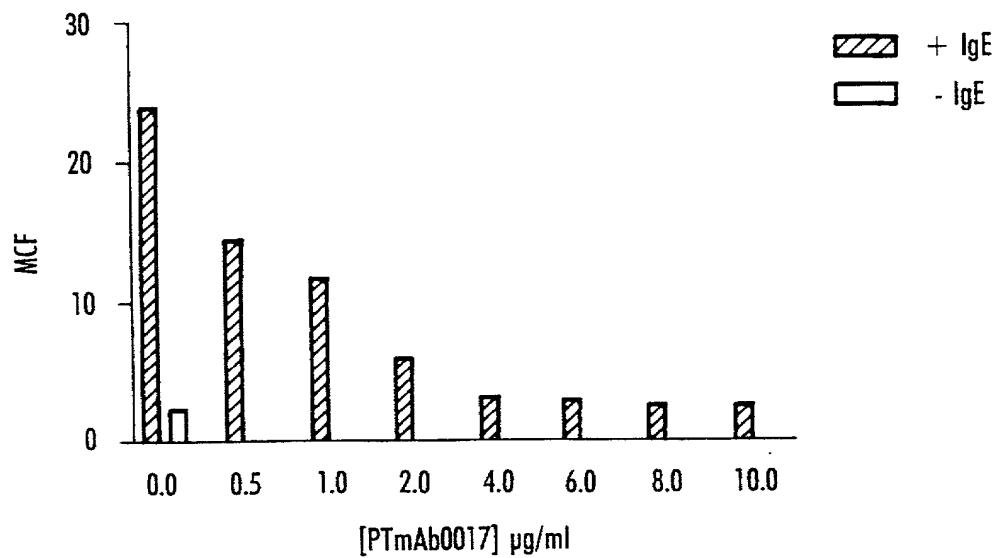
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**Fig. 25** The effect of PTmAb0011 on IgE binding to Fc $\epsilon$ RII on RPMI 8866 cells.

A



B



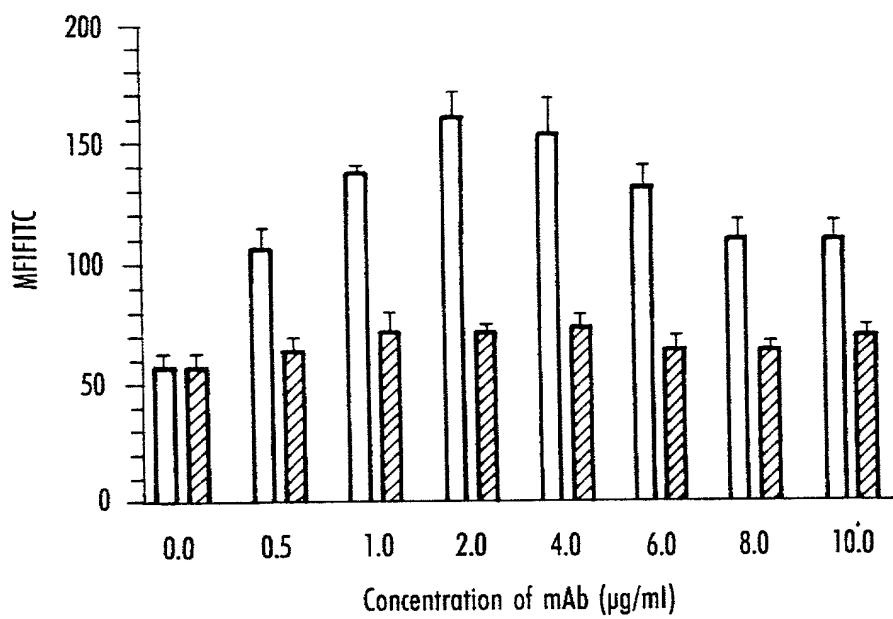
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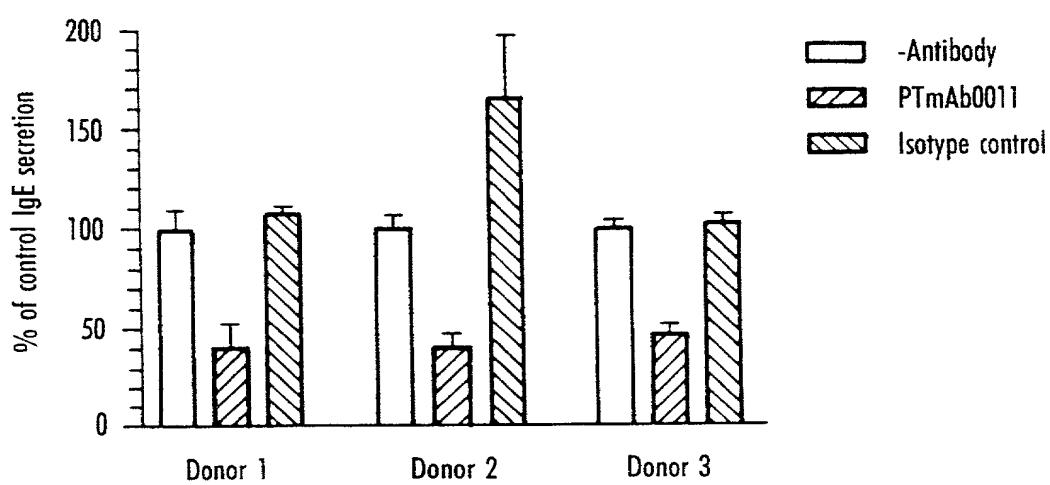
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**Fig. 26** Analysis of the effects of PTmAb0011 on IgE binding to Fc $\epsilon$ RII on primary human B-cells.



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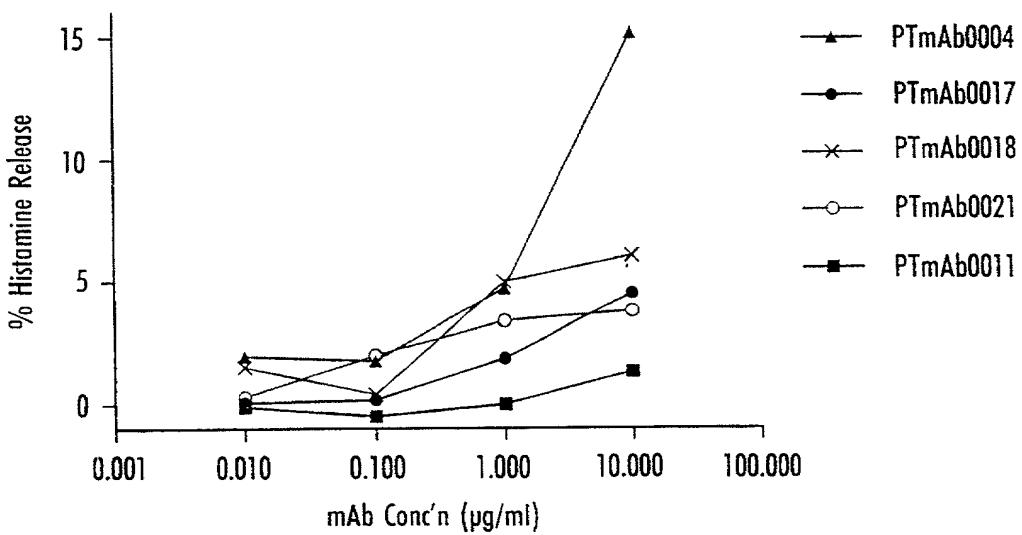
**Fig. 27** Effects of PTmAb0011 on IgE secretion from primary human B-cells.



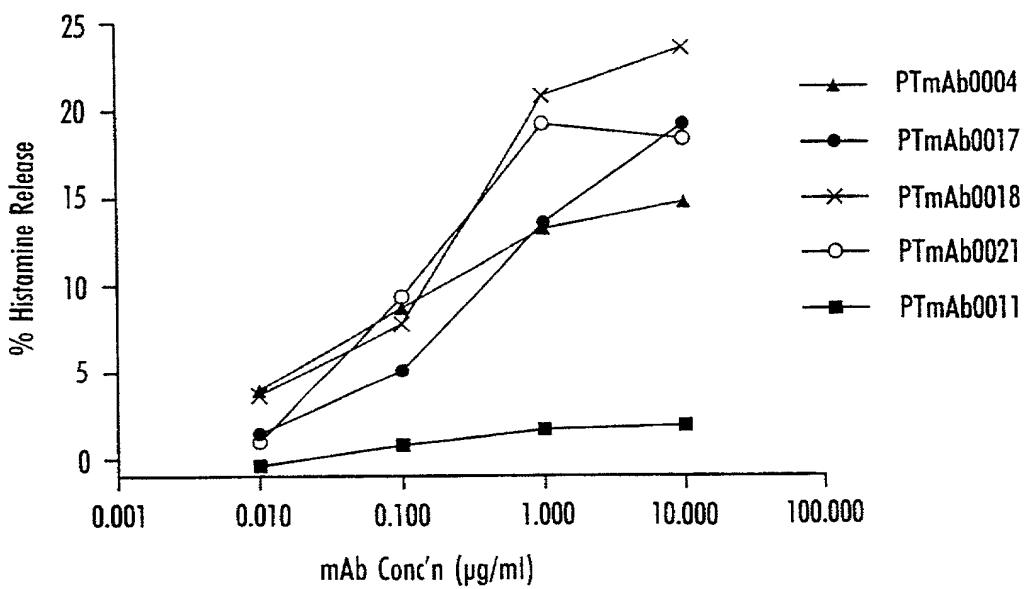
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**Fig. 28** Anaphylactogenicity of anti-human IgE monoclonal antibodies in allergic (A) and non-allergic (B) human basophils

A



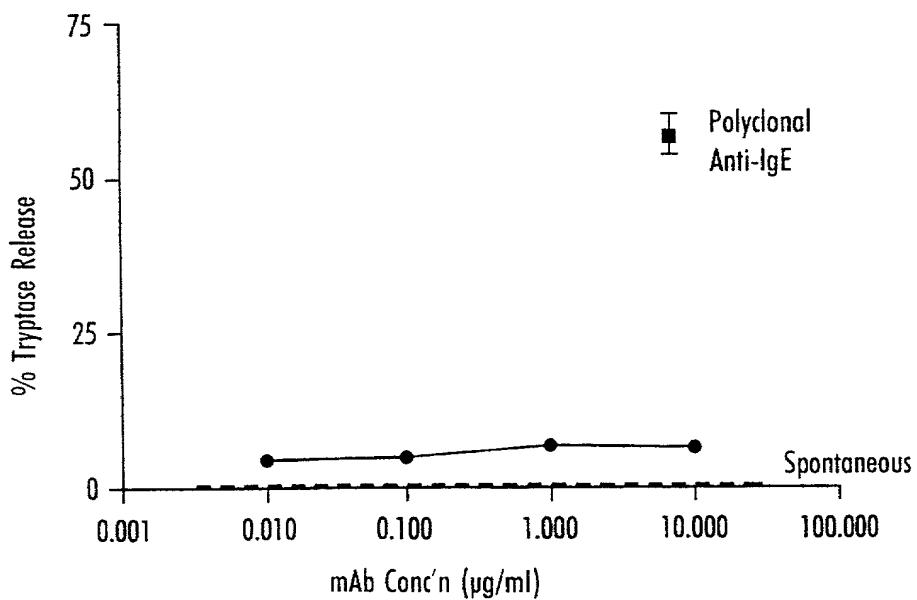
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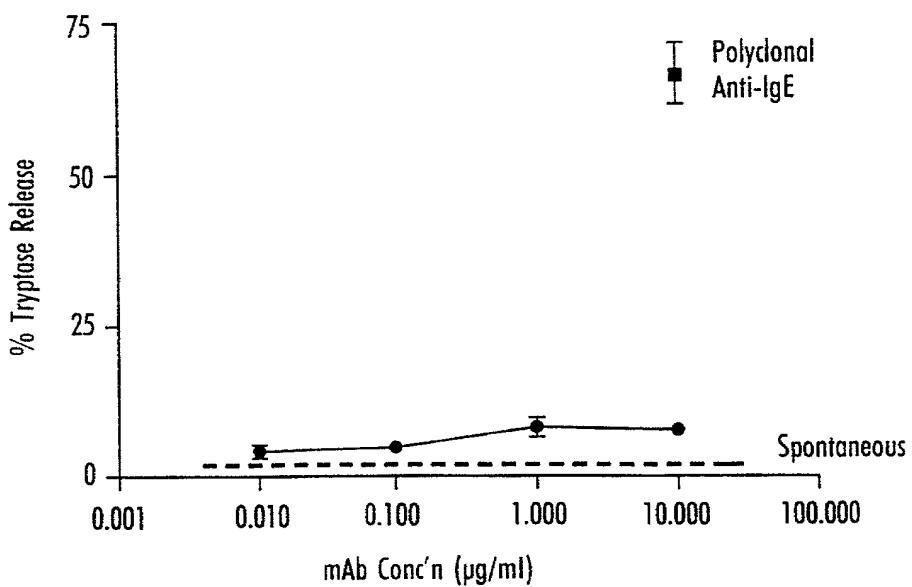
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**Fig. 29** Anaphylactogenicity of anti-human IgE antibodies in sensitised (A) and non-sensitised (B) human lung mast cells

A

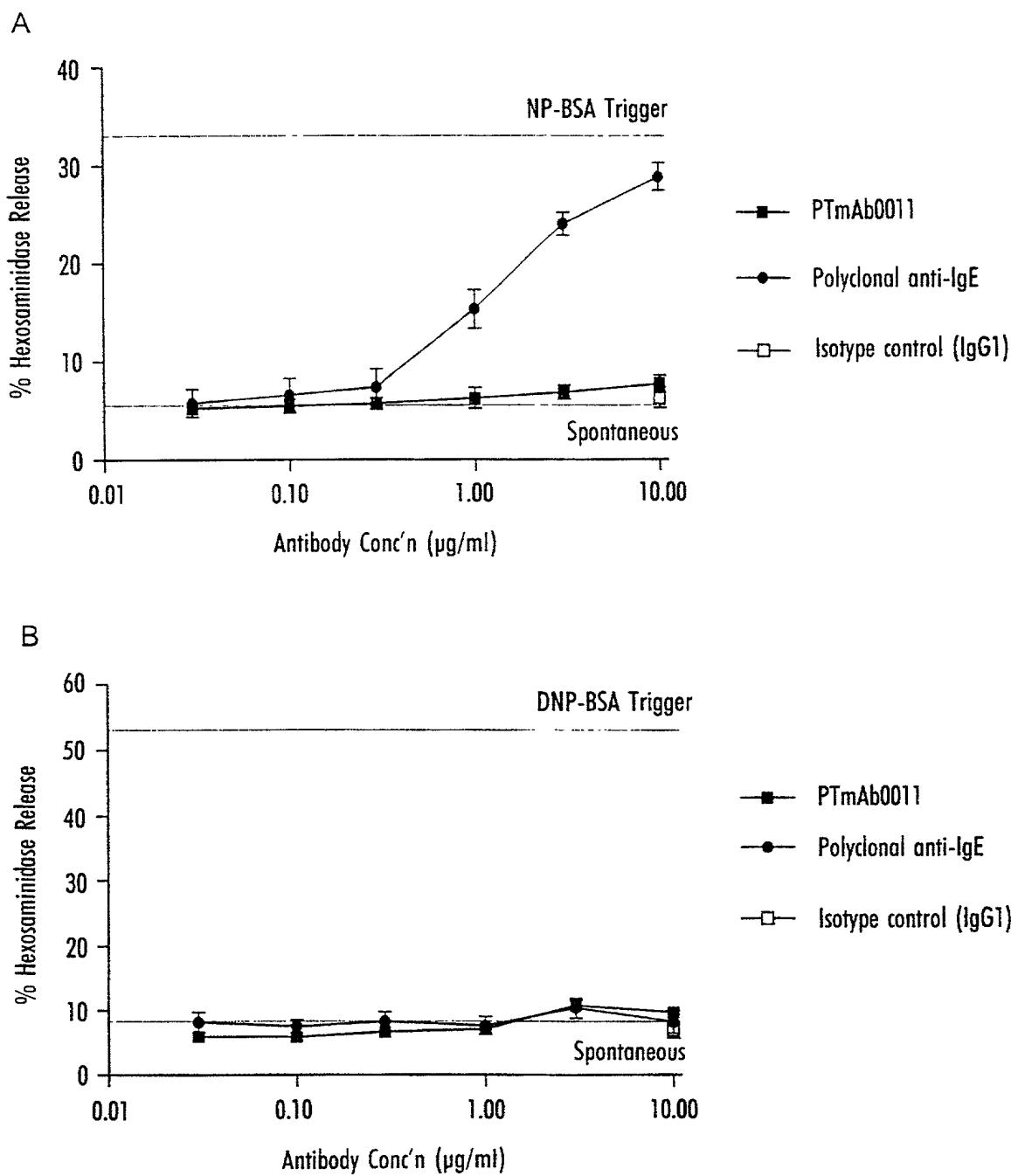


B



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**Fig. 30** Anaphylactogenicity of anti-human IgE antibodies in RBL J41 cells through human Fc $\epsilon$ RI (A) and mouse Fc $\epsilon$ RI (B)

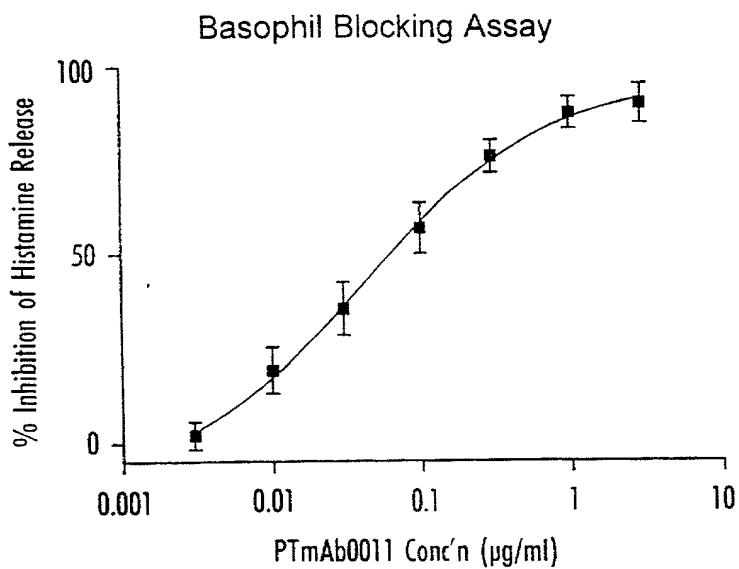


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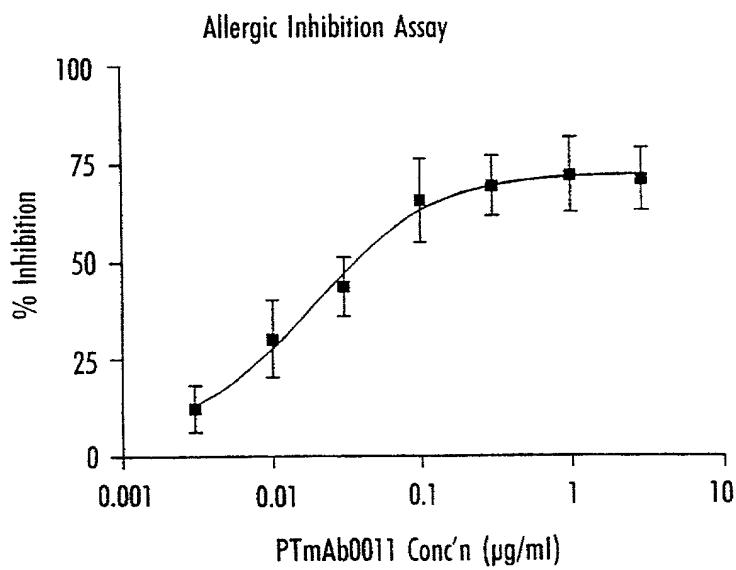
**Fig. 31**

Inhibition of allergen-triggered histamine release in human basophils by PTmAb0011

A

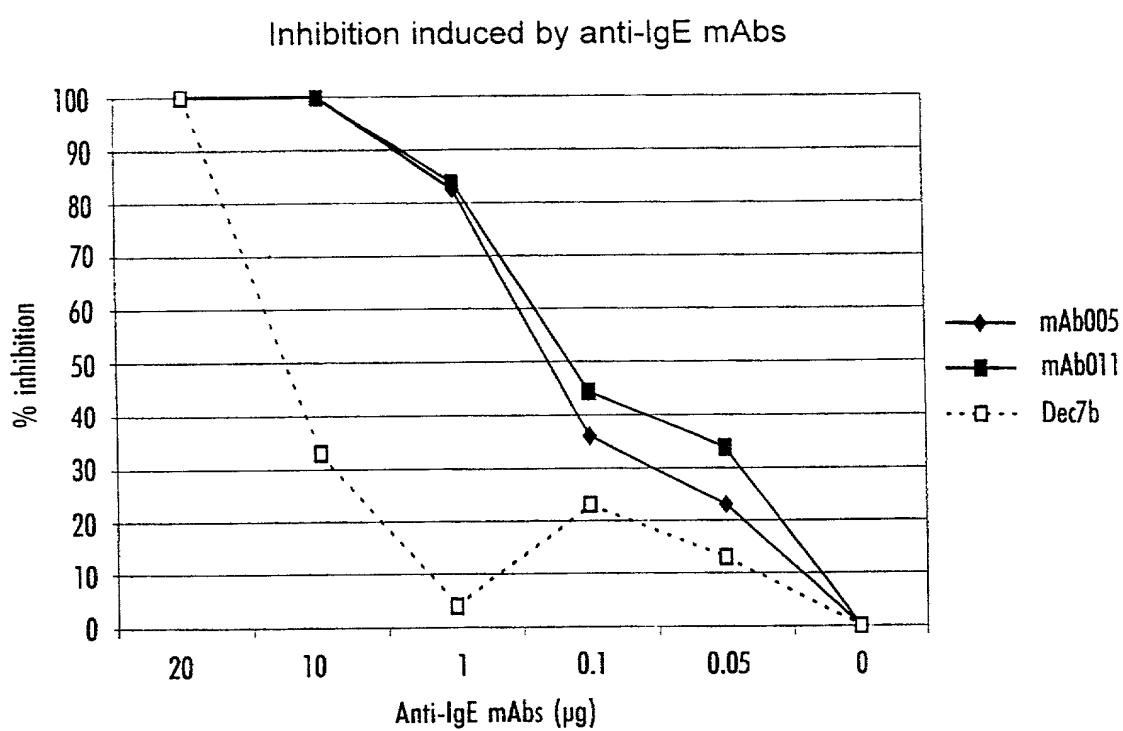


B



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**Fig. 32** Inhibition of passive cutaneous anaphylaxis in Monkey skin by PTmAb0011 and PTmAb0005.



## DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Epitopes or mimotopes derived from the C-Epsilon-2 domain of IGE, antagonists thereof, and their therapeutic uses

the specification of which (check one)

[ ] is attached hereto.

[ X ] was filed on 22 February 2000 as Serial No. PCT/EP00/01455  
and was amended on (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below any foreign application for patent or Inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

## Prior Foreign Application(s)

Number	Country	Filing Date	Priority Claimed
9907151.6	GB	29/03/1999	Yes No
9910537.1	GB	07/05/1999	Yes No
9910538.9	GB	07/05/1999	Yes No
9918594.4	GB	07/08/1999	Yes No
9918603.3	GB	07/08/1999	Yes No
9921046.0	GB	07/09/1999	Yes No
9921047.8	GB	07/09/1999	Yes No
9925619.0	GB	29/10/1999	Yes No
9927698.2	GB	23/11/1999	Yes No

I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below.

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As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Epitopes or mimotopes derived from the C-Epsilon-2 domain of IGE, antagonists thereof, and their therapeutic uses

the specification of which (check one)

[ ] is attached hereto.

[ X ] was filed on 22 February 2000 as Serial No. PCT/EP00/01455  
and was amended on (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below any foreign application for patent or Inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

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9907151.6	GB	29/03/1999	Yes No
9910537.1	GB	07/05/1999	Yes No
9910538.9	GB	07/05/1999	Yes No
9918594.4	GB	07/08/1999	Yes No
9918603.3	GB	07/08/1999	Yes No
9921046.0	GB	07/09/1999	Yes No
9921047.8	GB	07/09/1999	Yes No
9925619.0	GB	29/10/1999	Yes No
9927698.2	GB	23/11/1999	Yes No

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112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

Serial No.	Filing Date	Status
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I hereby appoint the practitioners associated with the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and direct that all correspondence be addressed to that Customer Number:

Customer Number 20462.

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Full Name of Inventor: Michael DYSON

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

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Citizenship: British

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King of Prussia, Pennsylvania 19406-0939

Full Name of Inventor: Martin FRIEDE

Inventor's Signature: Martin Date: 28 Sept 01

Residence: Cardiff, California, USA

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Corporate Intellectual Property - UW2220  
P.O. Box 1539  
King of Prussia, Pennsylvania 19406-0939

Full Name of Inventor: Judith GREENWOOD

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Cambridge, United Kingdom

Citizenship: British

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Full Name of Inventor: Ellen HEWITT

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Royston, Hertfordshire, United Kingdom

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Full Name of Inventor: Alan LAMONT

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

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Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
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Full Name of Inventor: Marcelle Paulette VAN MECHELEN

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Wagnelee, Belgium

Citizenship: Belgian

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Full Name of Inventor: Carlotta VINALS y de BASSOLS

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Brussels, Belgium

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Full Name of Inventor: Judith GREENWOOD

Inventor's Signature: Judith Greenwood Date: 2/10/01

Residence: Cambridge, United Kingdom

Citizenship: British

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Full Name of Inventor: Ellen HEWITT

Inventor's Signature: Ellen Hewitt Date: 2nd Oct 01

Residence: Royston, Hertfordshire, United Kingdom

Citizenship: British

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0223456789012345  
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Inventor's Signature: Randall Date: 2nd Oct 2001

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Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

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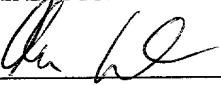
Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

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Full Name of Inventor: Alan LAMONT

Inventor's Signature:  Date: 17<sup>th</sup> Sept 01

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Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

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Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Colne, Huntingdon, United Kingdom

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Full Name of Inventor: William Gordon TURNELL

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Cambridge, United Kingdom

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
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Full Name of Inventor: Marcelle Paulette VAN MECHELEN

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Wagnelee, Belgium

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Full Name of Inventor: Sean MASON

Inventor's Signature: Sean Mason Date: 12th September 2001

Residence: Cambridge, United Kingdom

Citizenship: British

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full Name of Inventor: Michael DYSON

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

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Full Name of Inventor: Martin FRIEDE

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Cardiff, California, USA

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
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King of Prussia, Pennsylvania 19406-0939

Full Name of Inventor: Judith GREENWOOD

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Cambridge, United Kingdom

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
Corporate Intellectual Property - UW2220  
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King of Prussia, Pennsylvania 19406-0939

Full Name of Inventor: Ellen HEWITT

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Royston, Hertfordshire, United Kingdom

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
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King of Prussia, Pennsylvania 19406-0939

Full Name of Inventor: Alan LAMONT

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Croydon, Hertfordshire, United Kingdom

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
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P.O. Box 1539  
King of Prussia, Pennsylvania 19406-0939

Full Name of Inventor: Sean MASON

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Cambridge, United Kingdom

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
Corporate Intellectual Property - UW2220  
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King of Prussia, Pennsylvania 19406-0939

Full Name of Inventor: Roger RANDALL

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Colne, Huntingdon, United Kingdom

Citizenship: British

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Full Name of Inventor: William Gordon TURNELL

Inventor's Signature: Bill Turnell, Date: 10<sup>th</sup> Sept. 2001

Residence: Cambridge, United Kingdom

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
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King of Prussia, Pennsylvania 19406-0939

Full Name of Inventor: Marcelle Paulette VAN MECHELEN

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Wagnelee, Belgium

Citizenship: Belgian

Post Office Address: SmithKline Beecham Corporation  
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Full Name of Inventor: Carlotta VINALS y de BASSOLS

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Brussels, Belgium

Citizenship: Belgian

Post Office Address: SmithKline Beecham Corporation  
Corporate Intellectual Property - UW2220  
P.O. Box 1539  
King of Prussia, Pennsylvania 19406-0939

## DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Epitopes or mimotopes derived from the C-Epsilon-2 domain of IGE, antagonists thereof, and their therapeutic uses

the specification of which (check one)

[ ] is attached hereto.

[ X ] was filed on 22 February 2000 as Serial No. PCT/EP00/01455  
and was amended on (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below any foreign application for patent or Inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

## Prior Foreign Application(s)

Number	Country	Filing Date	Priority Claimed
9907151.6	GB	29/03/1999	Yes No
9910537.1	GB	07/05/1999	Yes No
9910538.9	GB	07/05/1999	Yes No
9918594.4	GB	07/08/1999	Yes No
9918603.3	GB	07/08/1999	Yes No
9921046.0	GB	07/09/1999	Yes No
9921047.8	GB	07/09/1999	Yes No
9925619.0	GB	29/10/1999	Yes No
9927698.2	GB	23/11/1999	Yes No

I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below.

Application Number Filing Date

I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s) or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, Section

112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

Serial No.	Filing Date	Status
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I hereby appoint the practitioners associated with the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and direct that all correspondence be addressed to that Customer Number:

Customer Number 20462.

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Full Name of Inventor: Michael DYSON

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Cambridge, United Kingdom

Citizenship: British

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Full Name of Inventor: Judith GREENWOOD

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Cambridge, United Kingdom

Citizenship: British

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Full Name of Inventor: Ellen HEWITT

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Full Name of Inventor: Alan LAMONT

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Croydon, Hertfordshire, United Kingdom

Citizenship: British

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Full Name of Inventor: Sean MASON

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

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Citizenship: British

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Full Name of Inventor: Roger RANDALL

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Colne, Huntingdon, United Kingdom

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
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King of Prussia, Pennsylvania 19406-0939

Full Name of Inventor: William Gordon TURNELL

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Cambridge, United Kingdom

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
Corporate Intellectual Property - UW2220  
P.O. Box 1539  
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Full Name of Inventor: Marcelle Paulette VAN MECHELEN

Inventor's Signature: Van Mechelen Date: 71<sup>st</sup> September 01

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Citizenship: Belgian

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Full Name of Inventor: Carlotta VINALS y de BASSOLS

Inventor's Signature: et Jules Date: 14.09.01

Residence: Brussels, Belgium

Citizenship: Belgian

Post Office Address: SmithKline Beecham Corporation  
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King of Prussia, Pennsylvania 19406-0939

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Full Name of Inventor: Michael DYSON

Inventor's Signature: M.R. Dyson Date: 6.9.01

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Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

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CA

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
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Full Name of Inventor: Judith GREENWOOD

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Cambridge, United Kingdom

*GBX*

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
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King of Prussia, Pennsylvania 19406-0939

400  
Full Name of Inventor: Ellen HEWITT

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Royston, Hertfordshire, United Kingdom

*GBX*

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
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500  
Full Name of Inventor: Alan LAMONT

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Croydon, Hertfordshire, United Kingdom

*GBX*

Citizenship: British

Post Office Address: SmithKline Beecham Corporation  
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King of Prussia, Pennsylvania 19406-0939

Full Name of Inventor: Sean MASON

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Cambridge, United Kingdom

*GBX*

Citizenship: British

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Full Name of Inventor: Roger RANDALL

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Colne, Huntingdon, United Kingdom

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Citizenship: British

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King of Prussia, Pennsylvania 19406-0939

Full Name of Inventor: William Gordon TURNELL

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Cambridge, United Kingdom

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Citizenship: British

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Full Name of Inventor: Marcelle Paulette VAN MECHELEN

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Wagnelee, Belgium

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Citizenship: Belgian

Post Office Address: SmithKline Beecham Corporation  
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Full Name of Inventor: Carlotta VINALS y de BASSOLS

Inventor's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Residence: Brussels, Belgium

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Citizenship: Belgian

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09/914088

PCT/EP00/01455

WO 00/50460

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Arg

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